**International Guidelines for Management of Sepsis and Septic Shock**

**Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2021**

**Appendix 2. Infection**

Laura Evans1, Andrew Rhodes2, Waleed Alhazzani3, Massimo Antonelli4, Craig M Coopersmith5, Craig French6, Flávia R. Machado7, Lauralyn Mcintyre8, Marlies Ostermann9, Hallie C. Prescott10, Christa Schorr11, Steven Simpson12, W Joost Wiersinga13, Fayez Alshamsi14, Derek C. Angus15, Yaseen Arabi16, Luciano Azevedo17, Richard Beale18, Gregory Beilman19, Emilie Belley-Cote20, Lisa Burry21,  Maurizio Cecconi22, John Centofanti23, Angel Coz Yataco24, Jan De Waele25, R. Phillip Dellinger26, Kent Doi27, Bin Du28, Elisa Estenssoro29, Ricard Ferrer30, Charles Gomersall31, Carol Hodgson32, Morten Hylander Møller33, Theodore Iwashyna34, Shevin Jacob35, Ruth Kleinpell36, Michael Klompas37, Younsuck Koh38, Anand Kumar39, Arthur Kwizera40, Suzana Lobo41, Henry Masur42, Steven McGloughlin43, Sangeeta Mehta44, Yatin Mehta45, Mervyn Mer46, Mark Nunnally47, Simon Oczkowski48, Tiffany Osborn49, Elizabeth Papathanassoglou50, Anders Perner51, Michael Puskarich52, Jason Roberts53, William Schweickert54, Maureen Seckel55, Jonathan Sevransky56, Charles L Sprung57, Tobias Welte58, Janice Zimmerman59, Mitchell Levy60.

**Affiliations**

Division of Pulmonary, Critical Care and Sleep Medicine, University of Washington, USA

Adult Critical Care, St George’s University Hospitals NHS Foundation Trust & St George’s University of London, London, UK

Department of Health Research Methods, Evidence, and Impact, McMaster University, Canada & Department of Medicine, McMaster University, Hamilton, Canada

Dipartimento di Scienze dell’ Emergenza  Anestesiologiche e della Rianimazione, Policlinico Universitario A. Gemelli IRCCS  Rome, Italy

Emory University School of Medicine, USA

Western Health, Melbourne, Australia

Federal University of Sao Paulo, Sao Paulo, Brazil

Ottawa Hospital, Ottawa, ON, Canada

Guy’s & St Thomas’ Hospital, London, England, UK

University of Michigan and VA Center for Clinical Management Research, USA

Cooper Health System, Camden, NJ, USA

University of Kansas Medical Center, Kansas City, KS, USA

1. Division of Infectious Diseases, Amsterdam UMC, University of Amsterdam, Amsterdam

Department of Internal Medicine, College of Medicine and Health Sciences, United Arab Emirates University, PO Box 17666, Al Ain, United Arab Emirates

University of Pittsburgh Critical Care Medicine CRISMA Laboratory, Pittsburgh, PA, USA

Intensive Care Department, Ministry of National Guard Health Affairs, King Saud Bin Abdulaziz University for Health Sciences, King Abdullah International Medical Research Center, Riyadh, Kingdom of Saudi Arabia

University of Sao Paulo, School of Medicine, Brazil

Guy’s & St Thomas’ Hospital, London, England, UK

University of Minnesota

Population Health Research Institute, Hamilton, Canada

Mount Sinai Hospital & University of Toronto (Leslie Dan Faculty of Pharmacy), Ontario Canada

Department of Anesthesia and Intensive care, Humanitas Clinical and Research Center, Rozzano, Milan, Italy.

Department of Anesthesia, McMaster University, Hamilton, Canada

Lexington Veterans Affairs Medical Center / University of Kentucky College of Medicine

Ghent University Hospital, Ghent, Belgium

Cooper Health System, Camden, NJ, USA

The University of Tokyo, Japan

Medical ICU, Peking Union Medical College Hospital, 1 Shuai Fu Yuan, Beijing 100730

Hospital Interzonal de Agudos San Martin de La Plata, Buenos Aires, Argentina

Intensive Care Department, Vall d'Hebron University Hospital, Vall d’Hebron Institut de Recerca. Barcelona, Spain.

Prince of Wales Hospital, Hong Kong, China

Australian and New Zealand Intensive Care Research Centre, Monash University, Australia

Copenhagen University Hospital Rigshospitalet, Department of Intensive Care 4131, Copenhagen, Denmark

University of Michigan Health System, USA

Liverpool School of Tropical Medicine, UK

Vanderbilt University Nashville TN, USA

Department of Medicine, Brigham and Women's Hospital, Boston MA; Department of Population Medicine, Harvard Medical School, and Harvard Pilgrim Health Care Institute, Boston MA, USA

ASAN Medical Center, University of Ulsan College of Medicine, Seoul, South Korea

University of Manitoba, Winnipeg, MB, Canada

Makerere University College of Health Sciences, Uganda

Intensive Care Division. Faculdade de Medicina de São José do Rio Preto, São Paulo- Brazil

Critical Care Medicine department, NIH Clinical Center, Bethedsa, MD, USA

Alfred Health, Australia

Medanta The Medicity, Gurugram, Haryana, India

Mount Sinai Hospital, Toronto, ON, Canada

Charlotte Maxeke Johannesburg Academic Hospital and Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

New York University School of Medicine, New York, NY, USA

Department of Medicine, McMaster University, Hamilton, Canada

Washington University School of Medicine, St. Louis, MO, USA

Faculty of Nursing, University of Alberta, Edmonton AB, Canada

Rigshospitalet, Copenhagen, Denmark

University of Minnesota / Hennepin County Medical Center

University of Queensland, Australia

University of Pennsylvania, USA

ChristianaCare, Newark, DE, USA

Emory University School of Medicine, USA

Faculty of Medicine, Hebrew University of Jerusalem, Israel and Department of Anesthesiology, Critical Care and Pain Medicine, Hadassah Medical Center, Jerusalem, Israel

Medizinische Hochschule Hannover and German Center of Lung Research (DZL), Germany

Houston Methodist Hospital, Houston, TX, USA

1. Warren Alpert School of Medicine at Brown University, Providence, Rhode Island & Rhode Island Hospital, Providence, Rhode Island.

Table of Contents

[Should clinical evaluation AND procalcitonin vs. clinical evaluation be used in be used to decide when to start antimicrobials in adults with suspected sepsis or septic shock? 4](#_Toc58438018)

[Evidence profile: Should clinical evaluation AND procalcitonin vs. clinical evaluation be used in be used to decide when to start antimicrobials in adults with suspected sepsis or septic shock? 4](#_Toc58438019)

[EtD: Summary of Judgments 6](#_Toc58438020)

[Type of Recommendation 7](#_Toc58438021)

[Should administration of early (within 1 hour of recognition of septic shock) empirical antimicrobials vs. administration of late (beyond 1 hour of recognition of septic shock) empirical antimicrobials be used in adults with septic shock? 8](#_Toc58438022)

[Should administration of early (within 1 hour of recognition of sepsis) empirical antimicrobials vs. Administration of late (beyond 1 hour of recognition of sepsis) empirical antimicrobials be used in adults with sepsis? 8](#_Toc58438023)

[Evidence profile for early antibiotics 8](#_Toc58438024)

[Forest plot Timing of antibiotics 9](#_Toc58438025)

[EtD: Summary of Judgements for Early Antibiotics 11](#_Toc58438026)

[Should shorter duration (as defined by the original trials) of antimicrobial therapy vs. longer duration (as defined by the original trials) of antimicrobial therapy be used in adults with sepsis or septic shock? 13](#_Toc58438027)

[Evidence profile Duration of Antibiotics 13](#_Toc58438028)

[Forest plot: Shorter versus longer duration of antimicrobial therapy according to syndrome in RCTs. Short-term mortality. 15](#_Toc58438029)

[EtD: Summary of Decisions: Duration of Antibiotics Recommendation 16](#_Toc58438030)

[Type of Recommendation 17](#_Toc58438031)

[Should daily assessment of de-escalation of antimicrobials vs. fixed duration of antimicrobial therapy (no daily assessment of de-escalation) be used in adults with sepsis or septic shock on antimicrobials? 18](#_Toc58438032)

[Evidence Profile 18](#_Toc58438033)

[Forest plot: De-escalation versus no de-escalation in patients with sepsis or septic shock (1 RCT and 12 observational studies). Short-term mortality. 20](#_Toc58438034)

[EtD. Summary of Decisions 21](#_Toc58438035)

[Type of Recommendation 22](#_Toc58438036)

[Should clinical evaluation AND procalcitonin to de-escalate/discontinue antimicrobials vs. clinical evaluation to de-escalate/discontinue antimicrobials be used in adults with sepsis or septic shock on antimicrobials? 23](#_Toc58438037)

[Evidence profile 23](#_Toc58438038)

[Forest plot: Use of procalcitonin to decide when to discontinue antimicrobials. RCTs. Short-term mortality 25](#_Toc58438039)

[EtD. Summary of Judgements 26](#_Toc58438040)

[Type of Recommendation 27](#_Toc58438041)

[Should two empirical antimicrobials with gram negative coverage vs. one empirical antimicrobial with gram negative coverage be used in adults with sepsis or septic shock? 28](#_Toc58438042)

[Should two empirical antimicrobials with different mechanisms of action to provide double-coverage of the most likely pathogen vs. empirical mono-active antimicrobial therapy be used in adults with sepsis or septic shock? 28](#_Toc58438043)

[Evidence profile 28](#_Toc58438044)

[EtD: Summary of Judgements 30](#_Toc58438045)

[Type of recommendation 31](#_Toc58438046)

[Should empirical antifungal therapy vs. no empirical antifungal therapy be used in adults with sepsis or septic shock at risk of fungal infection? 32](#_Toc58438047)

[Evidence profile 32](#_Toc58438048)

[EtD. Summary of Judgments 33](#_Toc58438049)

[Type of recommendation 34](#_Toc58438050)

[Should prolonged infusion of beta-lactams (maintenance) vs. bolus infusion of beta-lactams (maintenance) be used in adults with sepsis or septic shock? 35](#_Toc58438051)

[Evidence profile 35](#_Toc58438052)

[EtD. Summary of judgements 36](#_Toc58438053)

[Type of recommendation 37](#_Toc58438054)

[Should surgical source control within 12 hours vs. surgical source control beyond 12 hours be used in adults with sepsis or septic shock and a source amenable to source control? 38](#_Toc58438055)

[Evidence profile 38](#_Toc58438056)

[Forest plot: Early versus late source control in adults with sepsis or septic shock. Observational studies. Short-term mortality 40](#_Toc58438057)

[EtD. Summary of Judgments 41](#_Toc58438058)

[Should removal of indwelling catheters and foreign bodies vs. no removal of indwelling catheters and foreign bodies be used in adults with sepsis or septic shock potentially attributable to a catheter or foreign body? 43](#_Toc58438059)

[Table. Evidence profile 43](#_Toc58438060)

[Forest plot: Intravascular catheter removal versus watchful waiting in adults with suspected catheter related infection. Short-term mortality. 44](#_Toc58438061)

[EtD. Summary of Judgments 45](#_Toc58438062)

# Should clinical evaluation AND procalcitonin vs. clinical evaluation be used in be used to decide when to start antimicrobials in adults with suspected sepsis or septic shock?

## Evidence profile: Should clinical evaluation AND procalcitonin vs. clinical evaluation be used in be used to decide when to start antimicrobials in adults with suspected sepsis or septic shock?

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Quality assessment** | | | | | | | **№ of patients** | | **Effect** | | **Quality** | **Importance** |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **clinical evaluation AND procalcitonin** | **clinical evaluation** | **Relative (95% CI)** | **Absolute (95% CI)** |
| **Short-term mortality** | | | | | | | | | | | | |
| 3 | randomised trials | serious a | not serious | not serious | serious b | none | 251/892 (28.1%) | 248/877 (28.3%) | **RR 0.99** (0.86 to 1.15) | **3 fewer per 1,000** (from 40 fewer to 42 more) | ⨁⨁◯◯ LOW | CRITICAL |
| **Long-term mortality** | | | | | | | | | | | | |
| 0 |  |  |  |  |  |  | 0/0 | 0/0 | not estimable |  | - | CRITICAL |
| **ICU length of stay** | | | | | | | | | | | | |
| 3 | randomised trials | serious a | serious c | not serious | serious d | none | 892 | 877 | - | MD **0.19 higher** (0.98 lower to 1.36 higher) | ⨁◯◯◯ VERY LOW | CRITICAL |
| **Hospital length of stay** | | | | | | | | | | | | |
| 1 | randomised trials | serious a | not serious | not serious | very serious d | none | 30 | 30 | - | MD **7 lower** (26.24 lower to 12.24 higher) | ⨁◯◯◯ VERY LOW | CRITICAL |
| **Re-admission to hospital** | | | | | | | | | | | | |
| 0 |  |  |  |  |  |  | 0/0 | 0/0 | not estimable |  | - | CRITICAL |
| **Hospital free days** | | | | | | | | | | | | |
| 0 |  |  |  |  |  |  | 0 | 0 | - | **0**  (0 to 0 ) | - | CRITICAL |

**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

#### Explanations

a. No overall low risk of bias RCTs

b. 95% CI includes both increased and reduced mortality

c. Mean (SD) vales were calculated from median (IQR) values, and the converted results were not consistent between Lam 2018 SR and Peng 2019 SR

d. 95% CI includes both increased and reduced LOS

## EtD: Summary of Judgments

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable Effects** | **Trivial** | Small | Moderate | Large |  | Varies | Don't know |
| **Undesirable Effects** | Large | Moderate | Small | **Trivial** |  | Varies | Don't know |
| **Quality of evidence** | **Very low** | Low | Moderate | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | Possibly important uncertainty or variability | Probably no important uncertainty or variability | **No important uncertainty or variability** |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | **Does not favor either the intervention or the comparison** | Probably favors the intervention | Favors the intervention | Varies | Don't know |
| **Resources required** | Large costs | Moderate costs | Negligible costs and savings | Moderate savings | Large savings | Varies | **Don't know** |
| **Certainty of evidence of required resources** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **No included studies** |
| **Equity** | Reduced | Probably reduced | Probably no impact | Probably increased | Increased | **Varies** | Don't know |
| **Acceptability** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |
| **Feasibility** | No | Probably no | Probably yes | Yes |  | **Varies** | Don't know |

## Type of Recommendation

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Strong recommendation against the intervention | **Conditional recommendation against the intervention** | Conditional recommendation for either the intervention or the comparison | Conditional recommendation for the intervention | Strong recommendation for the intervention |
| ○ | **●** | ○ | ○ | ○ |

# Should administration of early (within 1 hour of recognition of septic shock) empirical antimicrobials vs. administration of late (beyond 1 hour of recognition of septic shock) empirical antimicrobials be used in adults with septic shock?

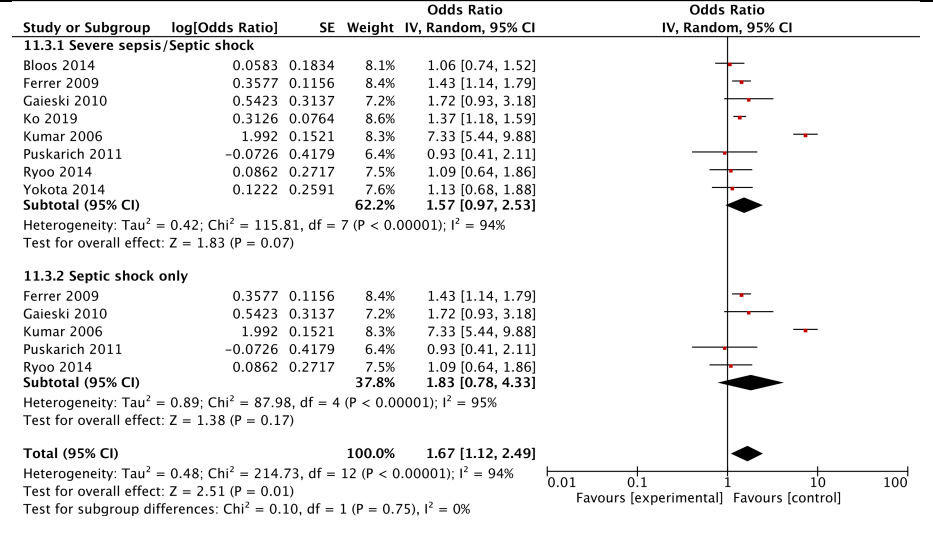
# Should administration of early (within 1 hour of recognition of sepsis) empirical antimicrobials vs. Administration of late (beyond 1 hour of recognition of sepsis) empirical antimicrobials be used in adults with sepsis?

## Evidence profile for early antibiotics

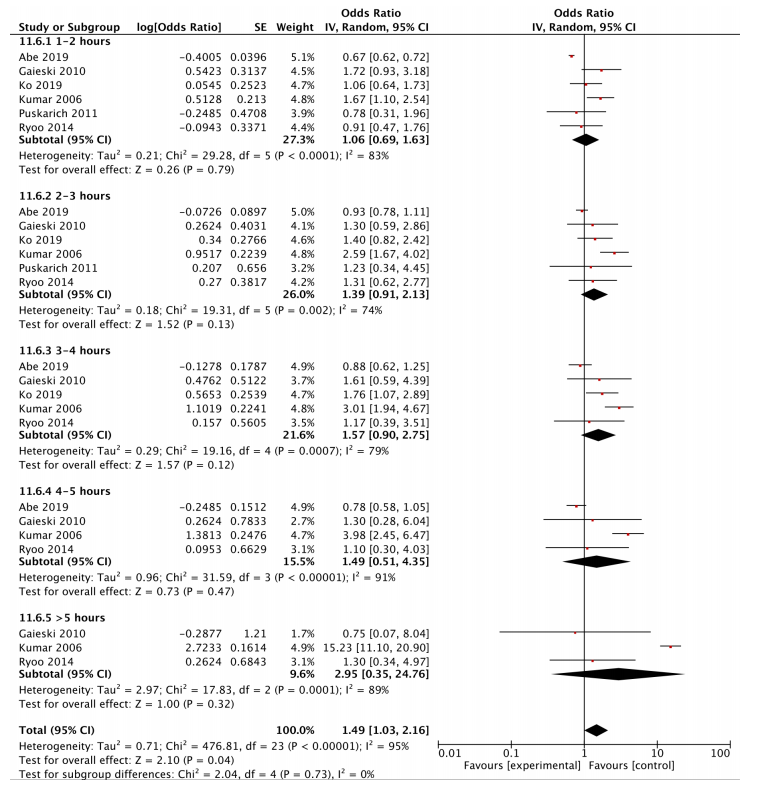
|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Outcomes** | **With late antibiotics**  **(beyond 1 hour)** | **With early antibiotics (within 1 hour)** | **Absolute difference** | **Relative effect (95% CI)** |
| **28-day mortality (%)**  1 RCT (n=2672) | 8.2% | 7.9% | 3 fewer per 1.000  (21 fewer to 20 more) | RR 0.96  (0.74 to 1.24) |
| **90-day mortality (%)**  1 RCT (n=2672) | 11.8% | 11.5% | 2 fewer per 1,000  (24 fewer to 25 more) | RR 0.98  (0.80 to 1.21) |

## Forest plot Timing of antibiotics

A) Antibiotics within versus beyond 1 hour in patients with severe sepsis/septic shock in observational studies. Mortality



B) Hourly delay in antibiotics in patients with sepsis and septic shock in observational studies. Mortality



## EtD: Summary of Judgements for Early Antibiotics

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable effects** | Trivial | Small | Moderate | **Large** |  | Varies | Don't know |
| **Undesirable effects** | Large | Moderate | Small | Trivial |  | **Varies** | Don't know |
| **Quality of evidence** | **Very low** | Low | Moderate | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | Possibly important uncertainty or variability | **Probably no important uncertainty or variability** | No important uncertainty or variability |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | **Probably favors the intervention** | Favors the intervention | Varies | Don't know |
| **Resources required** | Large costs | Moderate costs | Negligible costs and savings | Moderate savings | Large savings | Varies | **Don't know** |
| **Certainty of evidence of required resources** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **No included studies** |
| **Equity** | Reduced | Probably reduced | Probably no impact | Probably increased | Increased | Varies | **Don't know** |
| **Acceptability** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |
| **Feasibility** | No | Probably no | Probably yes | Yes |  | **Varies** | Don't know |

# Should shorter duration (as defined by the original trials) of antimicrobial therapy vs. longer duration (as defined by the original trials) of antimicrobial therapy be used in adults with sepsis or septic shock?

## Evidence profile Duration of Antibiotics

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Quality assessment** | | | | | | | **№ of patients** | | **Effect** | | **Quality** | **Importance** |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **shorter duration (as defined by the original trials ) of antimicrobial therapy** | **longer duration (as defined by the original trials) of antimicrobial therapy** | **Relative (95% CI)** | **Absolute (95% CI)** |
| **Short term mortality** | | | | | | | | | | | | |
| 16 | randomised trials | serious a | not serious | serious b | serious c | none | 185/2136 (8.7%) | 181/2100 (8.6%) | **RR 1.02** (0.85 to 1.22) | **2 more per 1,000** (from 13 fewer to 19 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| **Long term mortality (>90 days)** | | | | | | | | | | | | |
|  |  |  |  |  |  |  | 0/0 | 0/0 | not estimable |  | - | CRITICAL |
| **ICU length of stay** | | | | | | | | | | | | |
| 3 | randomised trials | serious a | not serious | serious d | serious e | none | 327 | 329 | - | MD **0.17 more** (1.5 fewer to 1.84 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| **Hospital length of stay** | | | | | | | | | | | | |
| 1 | randomised trials | serious f | not serious | serious d | very serious e | none | 14 | 16 | - | MD **1 fewer** (4.11 fewer to 2.11 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| **Re-admission to hospital** | | | | | | | | | | | | |
| 0 |  |  |  |  |  |  | 0/0 | 0/0 | not estimable |  | - | CRITICAL |
| **Hospital free days** | | | | | | | | | | | | |
| 0 |  |  |  |  |  |  | 0/0 | 0/0 | not estimable |  | - | CRITICAL |

**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

#### Explanations

a. Most RCTs had high risk of bias

b. Indirect population (different infectious conditions; not restricted to sepsis/septic shock)

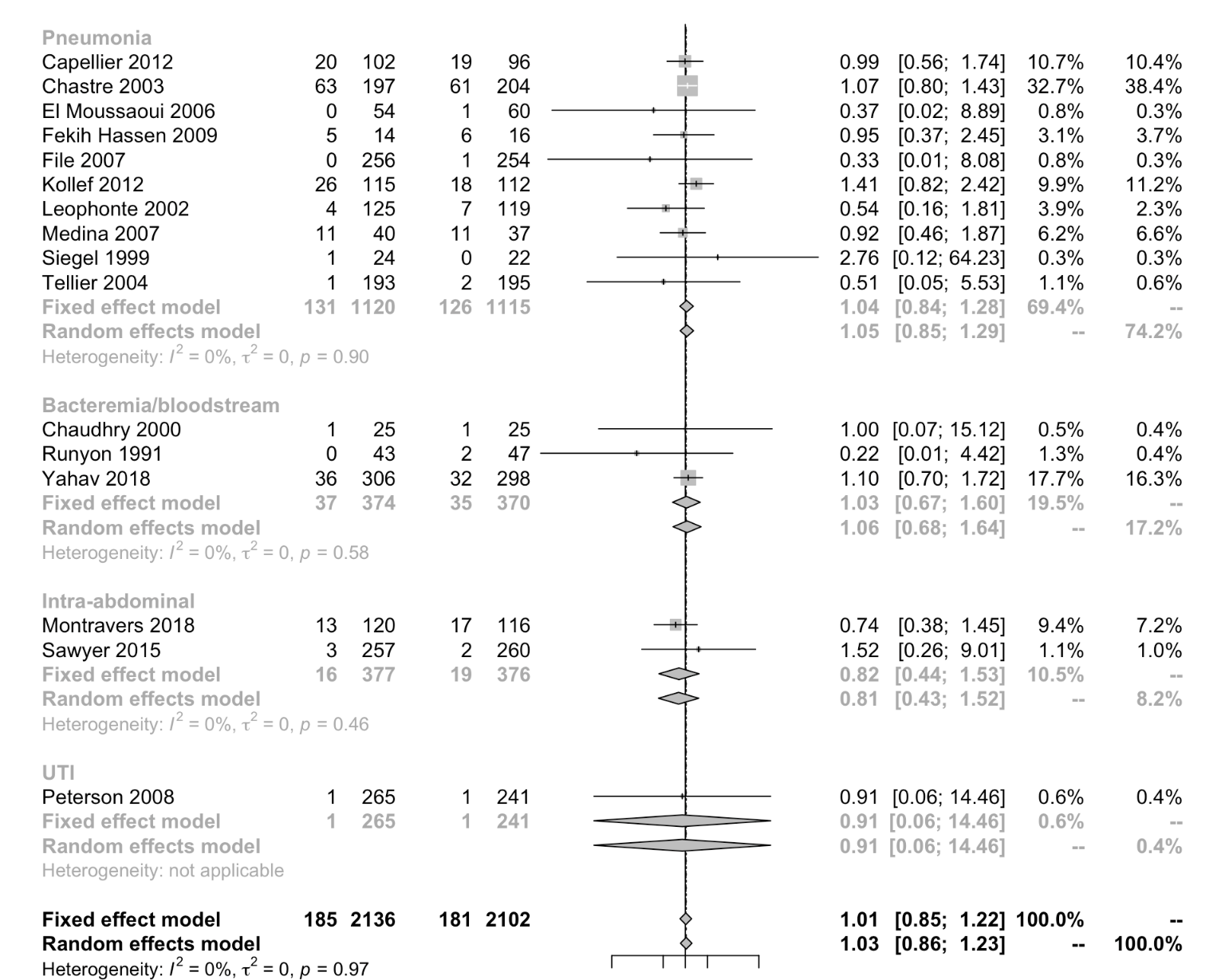
c. 95% CI includes both reduced and increased mortality

d. Indirect population (pneumonia)

e. 95% CI includes both reduced and increased LOS

f. High risk of bias RCT

## Forest plot: Shorter versus longer duration of antimicrobial therapy according to syndrome in RCTs. Short-term mortality.



## EtD: Summary of Decisions: Duration of Antibiotics Recommendation

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable Effects** | Trivial | **Small** | Moderate | Large |  | Varies | Don't know |
| **Undesirable Effects** | Large | **Moderate** | Small | Trivial |  | Varies | Don't know |
| **Certainty of evidence** | **Very low** | Low | Moderate | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | Possibly important uncertainty or variability | Probably no important uncertainty or variability | **No important uncertainty or variability** |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | **Does not favor either the intervention or the comparison** | Probably favors the intervention | Favors the intervention | Varies | Don't know |
| **Resources required** | Large costs | Moderate costs | Negligible costs and savings | **Moderate savings** | Large savings | Varies | Don't know |
| **Certainty of evidence of required resources** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **No included studies** |
| **Equity** | Reduced | Probably reduced | Probably no impact | Probably increased | Increased | Varies | **Don't know** |
| **Acceptability** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Feasibility** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |

## Type of Recommendation

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| strong recommendation against the intervention | conditional recommendation against the intervention | conditional recommendation for either the intervention or the comparison | **conditional recommendation for the intervention** | strong recommendation for the intervention |
| ○ | ○ | ○ | **●** | ○ |

# Should daily assessment of de-escalation of antimicrobials vs. fixed duration of antimicrobial therapy (no daily assessment of de-escalation) be used in adults with sepsis or septic shock on antimicrobials?

## Evidence Profile

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Quality assessment** | | | | | | | **№ of patients** | | **Effect** | | **Quality** | **Importance** |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **daily assessment of de-escalation of antimicrobials** | **fixed duration of antimicrobial therapy (no daily assessment of de-escalation)** | **Relative (95% CI)** | **Absolute (95% CI)** |
| **Short term mortality** | | | | | | | | | | | | |
| 13 | observational studies | serious a | serious b | not serious | not serious | none | 220/967 (22.8%) | 298/1001 (29.8%) | **RR 0.72** (0.57 to 0.91) | **83 fewer per 1,000** (from 128 fewer to 27 fewer) | ⨁◯◯◯ VERY LOW | CRITICAL |
| **Long term mortality (>90 days)** | | | | | | | | | | | | |
| 1 | observational studies | serious a | not serious | not serious | serious c | none | 31/117 (26.5%) | 30/112 (26.8%) | **RR 0.99** (0.64 to 1.52) | **3 fewer per 1,000** (from 96 fewer to 139 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| **ICU length of stay** | | | | | | | | | | | | |
| 6 | observational studies | serious a | serious b | not serious | serious d | none | 424 | 380 | - | MD **2.6 lower** (5.91 lower to 0.72 higher) | ⨁◯◯◯ VERY LOW | CRITICAL |
| **Hospital length of stay** | | | | | | | | | | | | |
| 4 | observational studies | serious a | not serious | not serious | serious e | none | 248 | 211 | - | MD **5.56 lower** (7.68 lower to 3.44 lower) | ⨁◯◯◯ VERY LOW | CRITICAL |
| **Re-admission to hospital** | | | | | | | | | | | | |
| - | - | - | - | - | - | - | - | - | - | - | - | CRITICAL |
| **Hospital free days** | | | | | | | | | | | | |
| - | - | - | - | - | - | - | - | - | - | - | - | CRITICAL |

**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

#### Explanations

a. Most studies had high risk of bias

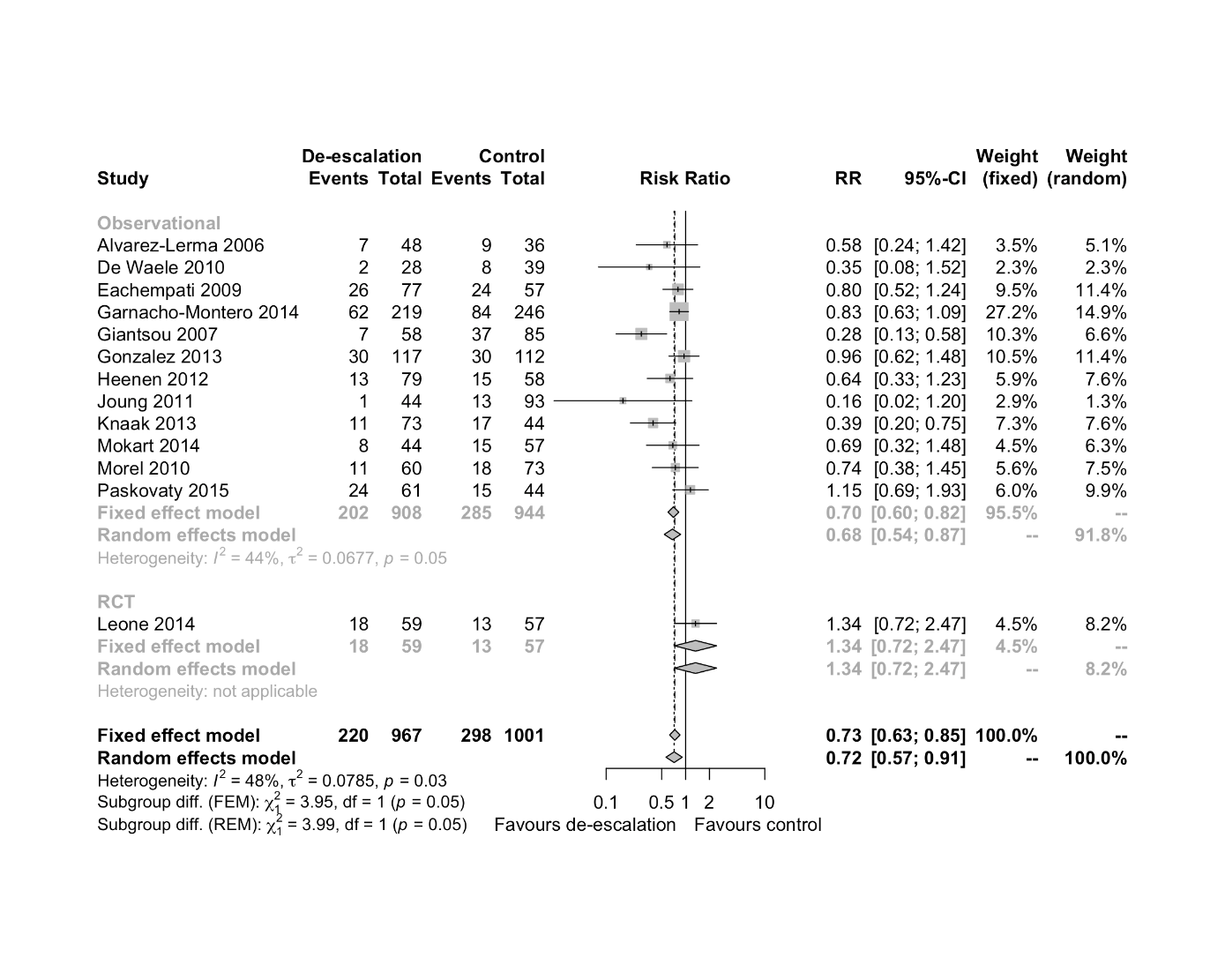
b. Differential results between data from observational studies and RCT

c. 95% CI includes both increased and reduced mortality

d. 95% CI includes both increased and reduced LOS

e. Wide 95% CI around the effect estimate

## Forest plot: De-escalation versus no de-escalation in patients with sepsis or septic shock (1 RCT and 12 observational studies). Short-term mortality.



## EtD. Summary of Decisions

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable Effects** | Trivial | Small | Moderate | **Large** |  | Varies | Don't know |
| **Undesirable Effects** | Large | Moderate | Small | **Trivial** |  | Varies | Don't know |
| **Certainty of evidence** | **Very low** | Low | Moderate | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | Possibly important uncertainty or variability | Probably no important uncertainty or variability | **No important uncertainty or variability** |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | **Probably favors the intervention** | Favors the intervention | Varies | Don't know |
| **Resources required** | Large costs | Moderate costs | Negligible costs and savings | **Moderate savings** | Large savings | Varies | Don't know |
| **Certainty of evidence of required resources** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **No included studies** |
| **Equity** | Reduced | Probably reduced | **Probably no impact** | Probably increased | Increased | Varies | Don't know |
| **Acceptability** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |
| **Feasibility** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |

## Type of Recommendation

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Strong recommendation against the intervention | Conditional recommendation against the intervention | Conditional recommendation for either the intervention or the comparison | **Conditional recommendation for the intervention** | Strong recommendation for the intervention |
| ○ | ○ | ○ | **●** | ○ |

# Should clinical evaluation AND procalcitonin to de-escalate/discontinue antimicrobials vs. clinical evaluation to de-escalate/discontinue antimicrobials be used in adults with sepsis or septic shock on antimicrobials?

## Evidence profile

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Quality assessment** | | | | | | | **№ of patients** | | **Effect** | | **Quality** | **Importance** |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **clinical evaluation AND procalcitonin to de-escalate/discontinue antimicrobials** | **clinical evaluation to de-escalate/discontinue antimicrobials** | **Relative (95% CI)** | **Absolute (95% CI)** |
| **Short term mortality** | | | | | | | | | | | | |
| 14 | randomised trials | serious a | not serious | not serious | not serious | none | 496/2500 (19.8%) | 552/2500 (22.1%) | **RR 0.89** (0.80 to 0.99) | **24 fewer per 1,000** (from 44 fewer to 2 fewer) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **Long term mortality (>90 days)** | | | | | | | | | | | | |
| 0 |  |  |  |  |  |  | 0/0 | 0/0 | not estimable |  | - | CRITICAL |
| **ICU length of stay** | | | | | | | | | | | | |
| 13 | randomised trials | serious a | serious b | not serious | serious c | none | 2449 | 2450 | - | MD **0.69 lower** (2.14 lower to 0.77 higher) | ⨁◯◯◯ VERY LOW | CRITICAL |
| **Hospital length of stay** | | | | | | | | | | | | |
| 10 | randomised trials | serious a | serious d | not serious | serious c | none | 2237 | 2245 | - | MD **1.19 lower** (3.5 lower to 1.12 higher) | ⨁◯◯◯ VERY LOW | CRITICAL |
| **Re-admission to hospital** | | | | | | | | | | | | |
| - | - | - | - | - | - | - | - | - | - | - | - | CRITICAL |

**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

#### Explanations

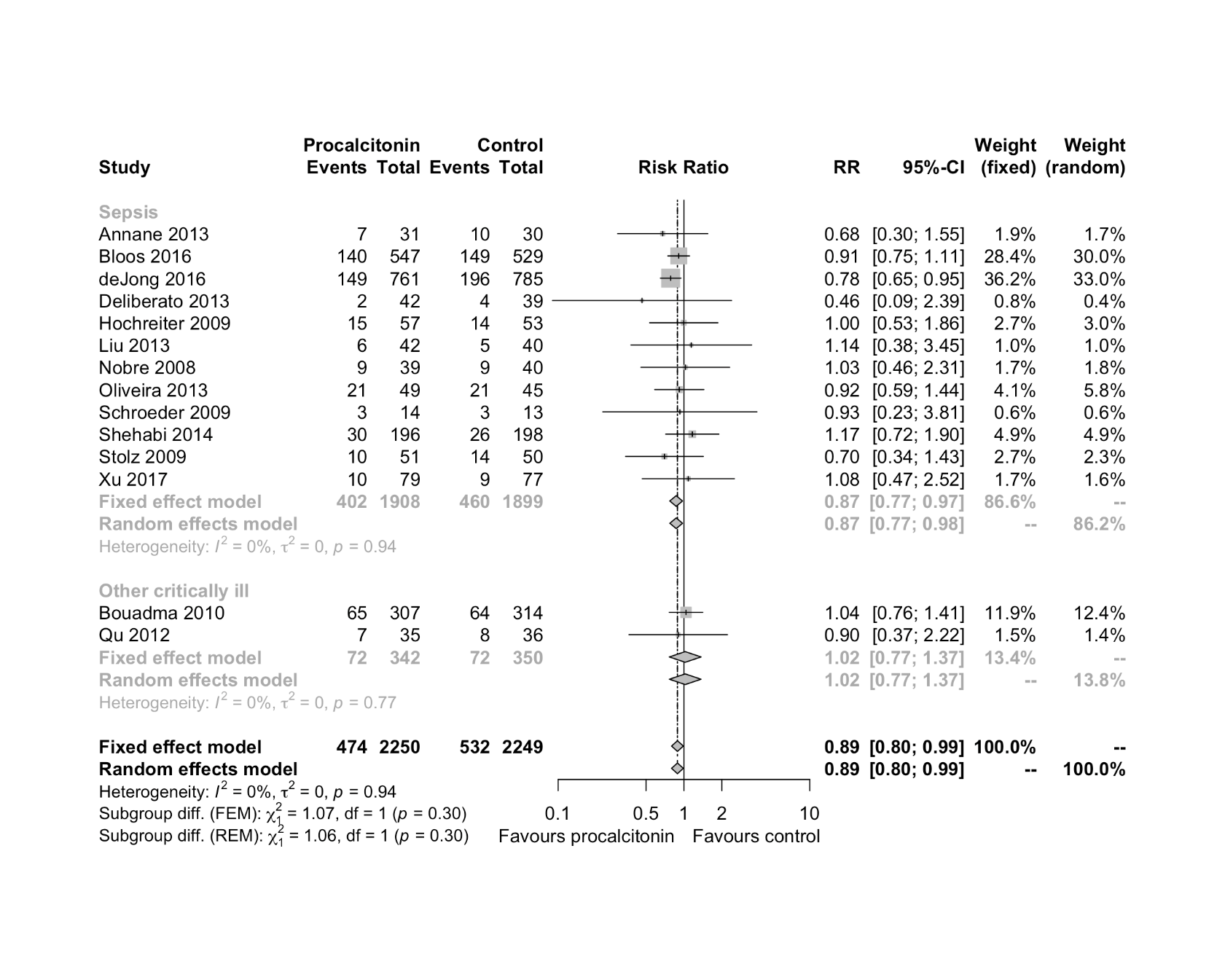
a. Most trials had high risk of bias

b. I2 =87%

c. 95% CI includes both increased and reduced LOS

d. I2 =83%

## Forest plot: Use of procalcitonin to decide when to discontinue antimicrobials. RCTs. Short-term mortality



## EtD. Summary of Judgements

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable effects** | Trivial | Small | **Moderate** | Large |  | Varies | Don't know |
| **Undesirable effects** | Large | Moderate | Small | **Trivial** |  | Varies | Don't know |
| **Quality of evidence** | Very low | **Low** | Moderate | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | **Possibly important uncertainty or variability** | Probably no important uncertainty or variability | No important uncertainty or variability |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | **Probably favors the intervention** | Favors the intervention | Varies | Don't know |
| **Resources required** | Large costs | Moderate costs | Negligible costs and savings | Moderate savings | Large savings | **Varies** | Don't know |
| **Certainty of evidence of required resources** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **No included studies** |
| **Equity** | Reduced | Probably reduced | Probably no impact | Probably increased | Increased | **Varies** | Don't know |
| **Acceptability** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |
| **Feasibility** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |

## Type of Recommendation

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Strong recommendation against the intervention | Conditional recommendation against the intervention | Conditional recommendation for either the intervention or the comparison | **Conditional recommendation for the intervention** | Strong recommendation for the intervention |
| ○ | ○ | ○ | **●** | ○ |

# Should two empirical antimicrobials with gram negative coverage vs. one empirical antimicrobial with gram negative coverage be used in adults with sepsis or septic shock?

# Should two empirical antimicrobials with different mechanisms of action to provide double-coverage of the most likely pathogen vs. empirical mono-active antimicrobial therapy be used in adults with sepsis or septic shock?

## Evidence profile

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Quality assessment** | | | | | | | | | | | | | | | | | | | | | **№ of patients** | | | | | | **Effect** | | | | | | **Quality** | | | **Importance** |
| **№ of studies** | | | **Study design** | | | **Risk of bias** | | **Inconsistency** | | | | **Indirectness** | | | **Imprecision** | | | **Other considerations** | | | **two empirical antimicrobials with different mechanisms of action to provide double-coverage of the most likely pathogen** | | | **empirical mono-active antimicrobial therapy** | | | **Relative (95% CI)** | | | **Absolute (95% CI)** | | |
| **Short term mortality** | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 10 | | | randomised trials | | | serious a | | not serious | | | | not serious | | | serious b | | | publication bias strongly suspected c | | | 269/1161 (23.2%) | | | 235/1106 (21.2%) | | | **RR 1.10** (0.94 to 1.28) | | | **21 more per 1,000** (from 13 fewer to 59 more) | | | ⨁◯◯◯ VERY LOW | | | CRITICAL |
| **Long term mortality (>90 days)** | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| - | | | - | | | - | | - | | | | - | | | - | | | - | | | - | | | - | | | - | | | - | | | - | | | CRITICAL |
| **ICU length of stay** | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 3 | | randomised trials | | | serious a | | | | not serious | | not serious | | | very serious d | | | none | | | 279 | | | 267 | | | - | | | MD **0.34 lower** (3.75 lower to 3.08 higher) | | | ⨁◯◯◯ VERY LOW | | | CRITICAL | |
| **Hospital length of stay** | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 1 | | randomised trials | | | serious a | | | | not serious | | not serious | | | very serious d | | | none | | | 71 | | | 69 | | | - | | | MD **1.6 higher** (5.29 lower to 8.49 higher) | | | ⨁◯◯◯ VERY LOW | | | CRITICAL | |
| **Re-admission to hospital** | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| - | | - | | | - | | | | - | | - | | | - | | | - | | | - | | | - | | | - | | | - | | | - | | | CRITICAL | |
| **Hospital free days** | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| - | - | | | - | | | - | | | - | | | - | | | - | | | - | | | - | | | - | | | - | | | - | | | CRITICAL | | |

**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

#### Explanations

a. Most trials had high risk of bias

b. 95% CI includes both increased and reduced mortality

c. Risk of small trial bias (publication bias) according to funnel plot

d. 95% CI includes both increased and reduced LOS

## EtD: Summary of Judgements

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable effects** | **Trivial** | Small | Moderate | Large |  | Varies | Don't know |
| **Undesirable effects** | Large | Moderate | **Small** | Trivial |  | Varies | Don't know |
| **Quality of evidence** | **Very low** | Low | Moderate | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | **Possibly important uncertainty or variability** | Probably no important uncertainty or variability | No important uncertainty or variability |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | **Does not favor either the intervention or the comparison** | Probably favors the intervention | Favors the intervention | Varies | Don't know |
| **Resources required** | Large costs | **Moderate costs** | Negligible costs and savings | Moderate savings | Large savings | Varies | Don't know |
| **Certainty of evidence of required resources** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **No included studies** |
| **Equity** | Reduced | Probably reduced | Probably no impact | Probably increased | Increased | Varies | **Don't know** |
| **Acceptability** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |
| **Feasibility** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |

## Type of recommendation

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Strong recommendation against the intervention | **Conditional recommendation against the intervention** | Conditional recommendation for either the intervention or the comparison | Conditional recommendation for the intervention | Strong recommendation for the intervention |
| ○ | **●** | ○ | ○ | ○ |

# Should empirical antifungal therapy vs. no empirical antifungal therapy be used in adults with sepsis or septic shock at risk of fungal infection?

## Evidence profile

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Quality assessment** | | | | | | | **№ of patients** | | **Effect** | | **Quality** | **Importance** |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **empirical antifungal therapy** | **no empirical antifungal therapy** | **Relative (95% CI)** | **Absolute (95% CI)** |
| **Short term mortality** | | | | | | | | | | | | |
| 7 | randomised trials | serious a | not serious | not serious | serious b | none | 140/487 (28.7%) | 147/503 (29.2%) | **RR 0.94** (0.68 to 1.30) | **18 fewer per 1,000** (from 94 fewer to 88 more) | ⨁⨁◯◯ LOW | CRITICAL |
| **Long Term Mortality (>90 days)** | | | | | | | | | | | | |
| - | - | - | - | - | - | - | - | - | - | - | - | CRITICAL |
| **ICU Length of Stay** | | | | | | | | | | | | |
| - | - | - | - | - | - | - | - | - | - | - | - | CRITICAL |
| **Hospital length of stay** | | | | | | | | | | | | |
| - | - | - | - | - | - | - | - | - | - | - | - | CRITICAL |
| **Re-admission to hospital** | | | | | | | | | | | | |
| - | - | - | - | - | - | - | - | - | - | - | - | CRITICAL |
| **Hospital free days** | | | | | | | | | | | | |
| - | - | - | - | - | - | - | - | - | - | - | - | CRITICAL |

**CI:** Confidence interval; **RR:** Risk ratio

#### Explanations

a. Most trials had overall high risk of bias

b. 95% CI includes both increased and reduced mortality

## EtD. Summary of Judgments

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable Effects** | Trivial | **Small** | Moderate | Large |  | Varies | Don't know |
| **Undesirable Effects** | Large | Moderate | Small | Trivial |  | Varies | **Don't know** |
| **Certainty of evidence** | Very low | **Low** | Moderate | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | Possibly important uncertainty or variability | Probably no important uncertainty or variability | **No important uncertainty or variability** |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | **Does not favor either the intervention or the comparison** | Probably favors the intervention | Favors the intervention | Varies | Don't know |
| **Resources required** | Large costs | **Moderate costs** | Negligible costs and savings | Moderate savings | Large savings | Varies | Don't know |
| **Certainty of evidence of required resources** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **No included studies** |
| **Equity** | Reduced | Probably reduced | Probably no impact | Probably increased | Increased | Varies | **Don't know** |
| **Acceptability** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |
| **Feasibility** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |

## Type of recommendation

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Strong recommendation against the intervention | Conditional recommendation against the intervention | **Conditional recommendation for either the intervention or the comparison** | Conditional recommendation for the intervention | Strong recommendation for the intervention |
| ○ | ○ | **●** | ○ | ○ |

# Should prolonged infusion of beta-lactams (maintenance) vs. bolus infusion of beta-lactams (maintenance) be used in adults with sepsis or septic shock?

## Evidence profile

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Quality assessment** | | | | | | | **№ of patients** | | **Effect** | | **Quality** | **Importance** |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **prolonged infusion of beta-lactams (maintenance)** | **bolus infusion of beta-lactams (maintenance)** | **Relative (95% CI)** | **Absolute (95% CI)** |
| **Short term mortality** | | | | | | | | | | | | |
| 17 | randomised trials | serious a | not serious | not serious | not serious | none | 110/792 (13.9%) | 161/805 (20.0%) | **RR 0.70** (0.57 to 0.87) | **60 fewer per 1,000** (from 86 fewer to 26 fewer) | ⨁⨁⨁◯ MODERATE | CRITICAL |
| **Long term mortality (>90 days)** | | | | | | | | | | | | |
| - | - | - | - | - | - | - | - | - | - | - | - | CRITICAL |
| **ICU length of stay** | | | | | | | | | | | | |
| - | - | - | - | - | - | - | - | - | - | - | - | CRITICAL |
| **Hospital length of stay** | | | | | | | | | | | | |
| - | - | - | - | - | - | - | - | - | - | - | - | CRITICAL |
| **Re-admission to hospital** | | | | | | | | | | | | |
| - | - | - | - | - | - | - | - | - | - | - | - | CRITICAL |
| **Hospital free days** | | | | | | | | | | | | |
| - | - | - | - | - | - | - | - | - | - | - | - | CRITICAL |

**CI:** Confidence interval; **RR:** Risk ratio

#### Explanations

a. Most trials had high risk of bias

## EtD. Summary of judgements

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable Effects** | Trivial | Small | Moderate | **Large** |  | Varies | Don't know |
| **Undesirable Effects** | Large | Moderate | Small | Trivial |  | Varies | **Don't know** |
| **Certainty of evidence** | Very low | Low | **Moderate** | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | Possibly important uncertainty or variability | Probably no important uncertainty or variability | **No important uncertainty or variability** |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | **Favors the intervention** | Varies | Don't know |
| **Resources required** | Large costs | Moderate costs | **Negligible costs and savings** | Moderate savings | Large savings | Varies | Don't know |
| **Certainty of evidence of required resources** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **No included studies** |
| **Equity** | Reduced | Probably reduced | Probably no impact | Probably increased | Increased | **Varies** | Don't know |
| **Acceptability** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Feasibility** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |

## Type of recommendation

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Strong recommendation against the intervention | Conditional recommendation against the intervention | Conditional recommendation for either the intervention or the comparison | **Conditional recommendation for the intervention** | Strong recommendation for the intervention |
| ○ | ○ | ○ | **●** | ○ |

# Should surgical source control within 12 hours vs. surgical source control beyond 12 hours be used in adults with sepsis or septic shock and a source amenable to source control?

## Evidence profile

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Certainty assessment** | | | | | | | **№ of patients** | | **Effect** | | **Certainty** | **Importance** |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **surgical source control within 12 hours** | **surgical source control beyond 12 hours** | **Relative (95% CI)** | **Absolute (95% CI)** |
| **Short term mortality** | | | | | | | | | | | | |
| 4 | observational studies | not serious | serious a | not serious | serious b | none | 808/3062 (26.4%) | 401/1338 (30.0%) | **RR 0.86** (0.66 to 1.11) | **42 fewer per 1,000** (from 102 fewer to 33 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| **Long term mortality (>90 days)** | | | | | | | | | | | | |
| - | - | - | - | - | - | - | - | - | - | - | - | CRITICAL |
| **ICU length of stay** | | | | | | | | | | | | |
| 1 | observational studies | not serious | not serious | not serious | serious c | none | 825 | 265 | - | MD **0.5 lower** (2.62 lower to 1.62 higher) | ⨁◯◯◯ VERY LOW | CRITICAL |
| **Hospital length of stay** | | | | | | | | | | | | |
| 1 | observational studies | not serious | not serious | not serious | serious c | none | 825 | 265 | - | MD **0.3 higher** (3.69 lower to 4.29 higher) | ⨁◯◯◯ VERY LOW | CRITICAL |
| **Re-admission to hospital** | | | | | | | | | | | | |
| - | - | - | - | - | - | - | - | - | - | - | - | CRITICAL |
| **Hospital free days** | | | | | | | | | | | | |
| - | - | - | - | - | - | - | - | - | - | - | - | CRITICAL |

**CI:** Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

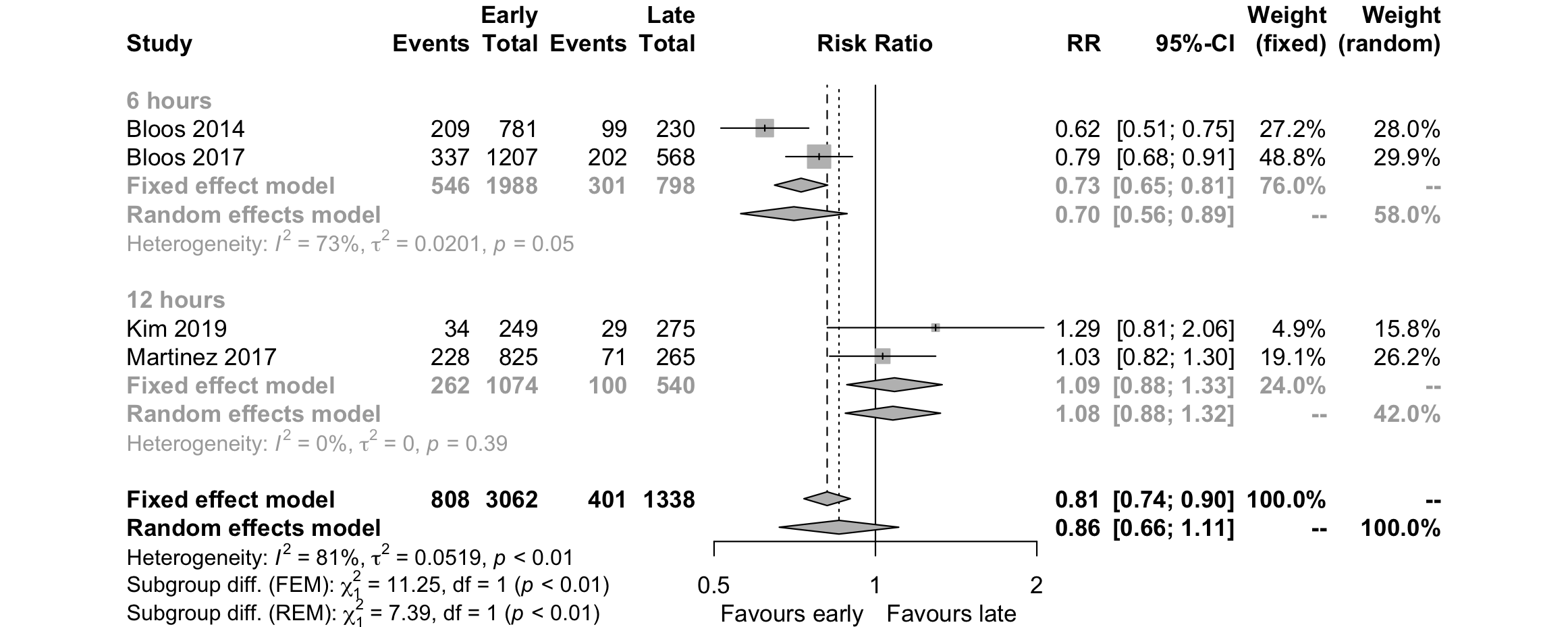
#### Explanations

a. Difference between a cut-off of 6 vs. 12 hours

b. 95% CI includes both increased and reduced mortality

c. 95% CI includes both increased and reduced LOS

## Forest plot: Early versus late source control in adults with sepsis or septic shock. Observational studies. Short-term mortality



## EtD. Summary of Judgments

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable Effects** | Trivial | Small | **Moderate** | Large |  | Varies | Don't know |
| **Undesirable Effects** | Large | Moderate | Small | **Trivial** |  | Varies | Don't know |
| **Certainty of evidence** | **Very low** | Low | Moderate | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | Possibly important uncertainty or variability | Probably no important uncertainty or variability | **No important uncertainty or variability** |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | **Probably favors the intervention** | Favors the intervention | Varies | Don't know |
| **Resources required** | Large costs | Moderate costs | Negligible costs and savings | **Moderate savings** | Large savings | Varies | Don't know |
| **Certainty of evidence of required resources** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **No included studies** |
| **Equity** | Reduced | Probably reduced | **Probably no impact** | Probably increased | Increased | Varies | Don't know |
| **Acceptability** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Feasibility** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |

# Should removal of indwelling catheters and foreign bodies vs. no removal of indwelling catheters and foreign bodies be used in adults with sepsis or septic shock potentially attributable to a catheter or foreign body?

## Table. Evidence profile

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Quality assessment** | | | | | | | **№ of patients** | | **Effect** | | **Quality** | **Importance** |
| **№ of studies** | **Study design** | **Risk of bias** | **Inconsistency** | **Indirectness** | **Imprecision** | **Other considerations** | **removal of indwelling catheters and foreign bodies** | **no removal of indwelling catheters and foreign bodies** | **Relative (95% CI)** | **Absolute (95% CI)** |
| **Short term mortality** | | | | | | | | | | | | |
| 3 | observational studies | not serious | serious a | not serious | serious b | none | 69/294 (23.5%) | 44/220 (20.0%) | **RR 0.99** (0.55 to 1.79) | **2 fewer per 1,000** (from 90 fewer to 158 more) | ⨁◯◯◯ VERY LOW | CRITICAL |
| **Long term mortality (>90 days)** | | | | | | | | | | | | |
| - | - | - | - | - | - | - | - | - | - | - | - | CRITICAL |
| **ICU length of stay** | | | | | | | | | | | | |
| - | - | - | - | - | - | - | - | - | - | - | - | CRITICAL |
| **Hospital length of stay** | | | | | | | | | | | | |
| - | - | - | - | - | - | - | - | - | - | - | - | CRITICAL |
| **Re-admission to hospital** | | | | | | | | | | | | |
| - | - | - | - | - | - | - | - | - | - | - | - | CRITICAL |
| **Hospital free days** | | | | | | | | | | | | |
| - | - | - | - | - | - | - | - | - | - | - | - | CRITICAL |

**CI:** Confidence interval; **RR:** Risk ratio

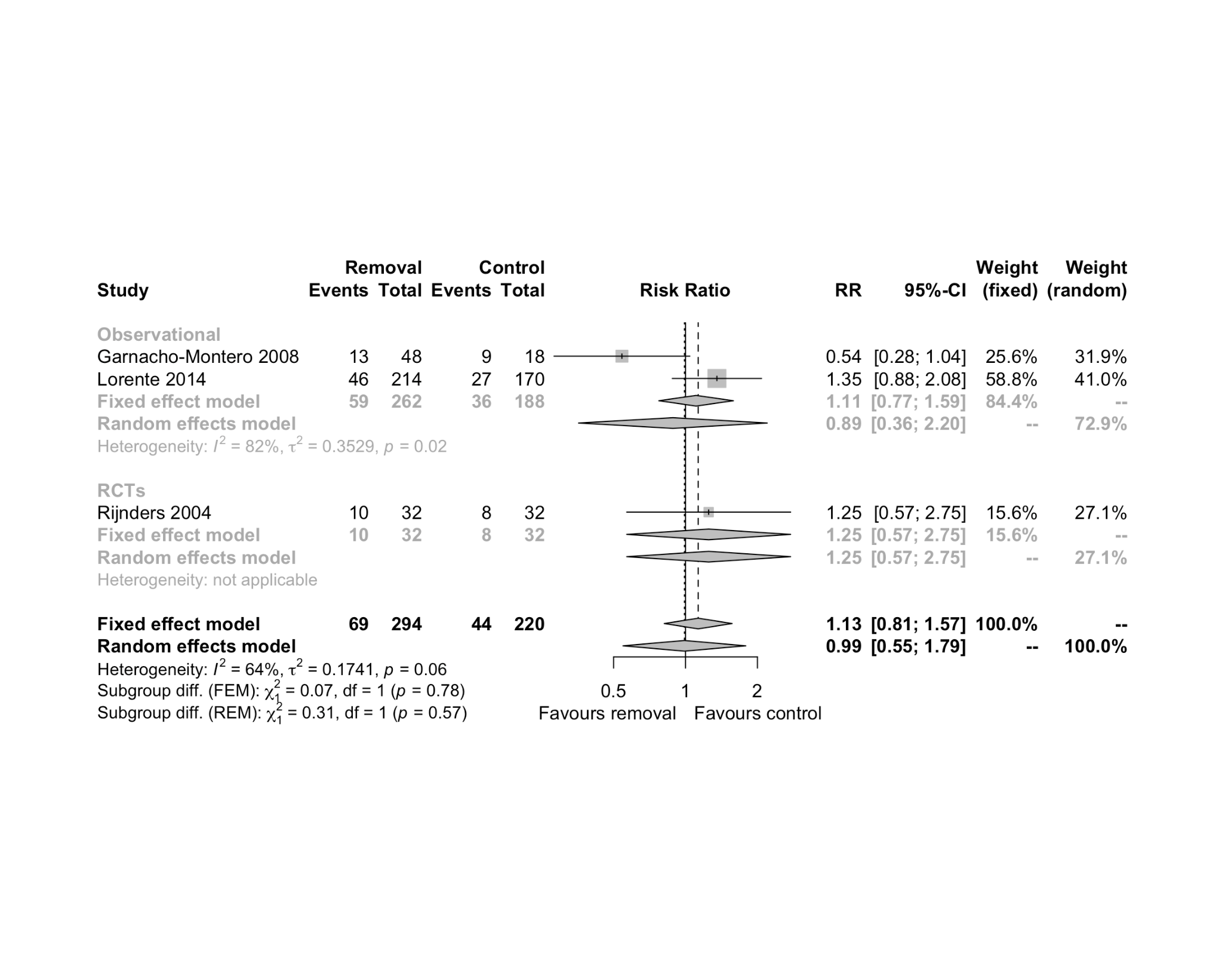
#### Explanations

a. I2 64%

b. 95% CI includes both increased and reduced mortality

c. High risk of bias trial

## Forest plot: Intravascular catheter removal versus watchful waiting in adults with suspected catheter related infection. Short-term mortality.



## EtD. Summary of Judgments

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable Effects** | **Trivial** | Small | Moderate | Large |  | Varies | Don't know |
| **Undesirable Effects** | Large | Moderate | Small | Trivial |  | Varies | **Don't know** |
| **Certainty of evidence** | **Very low** | Low | Moderate | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | Possibly important uncertainty or variability | **Probably no important uncertainty or variability** | No important uncertainty or variability |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | **Does not favor either the intervention or the comparison** | Probably favors the intervention | Favors the intervention | Varies | Don't know |
| **Resources required** | Large costs | Moderate costs | Negligible costs and savings | Moderate savings | Large savings | **Varies** | Don't know |
| **Certainty of evidence of required resources** | Very low | Low | Moderate | High |  |  | **No included studies** |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **No included studies** |
| **Equity** | Reduced | Probably reduced | Probably no impact | Probably increased | Increased | Varies | **Don't know** |
| **Acceptability** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |
| **Feasibility** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |